Investigating Noroviruses: A Case Study

David Bergmire-Sweat, MPH
North Carolina Department of Health and Human Services
Norovirus Facts

- Small, round-structured viruses from *Caliciviridae* family
- First recognized as pathogenic cause of gastroenteritis in 1968, Norwalk, Ohio
- Transmitted via fecal-oral route
- Highly contagious—as few as 10 viral particles can cause infection
Symptoms

- Incubation period ~ 24-48 hours, can be less
- Vomiting
- Watery non-bloody diarrhea
- Abdominal cramps
- Nausea
- Low-grade fever
- Symptoms typically resolve ~ 24-60 hours (1-3 days)
Documented Modes of Transmission

- Foodhandler contamination of items in restaurant
- Daycare centers
- Secondary person-to-person
- Aerosolized (vomiting and diarrhea)
- Cleaning up after ill person in a bathroom
Immunity & Epidemiology

- Seems to be strain-specific and temporary (few months)
- CDC estimates 23 million cases of acute gastroenteritis annually in U.S. due to noroviruses
- CDC estimates noroviruses cause ~50% of all foodborne disease outbreaks
Detection

- Best method is via reverse transcriptase polymerase chain reaction (RT-PCR)
- Viral RNA
- Adults can shed viral particles for up to 2 weeks after symptoms resolve
- Infants and toddlers may shed longer
Case Study

- Small state university north of Houston, TX
- Student body ~ 10,000 students
- 2,054 students owned meal plans
- 125 students present to student health center and local hospital with gastrointestinalitis in 24 hr period
Symptoms

- 125 ill students on March 10-11 1998
- 23 admitted to hospital
- 91% reported vomiting
- 85% reported diarrhea (3+ loose stools in 24 hours)
- 68% reported abdominal cramps
Epidemic Curve

Cases by Onset Date
62 stool samples sent to Texas Department of Health Lab in Austin

All negative for *Salmonella, Shigella, Campylobacter, Yersinia, E. coli O157:H7, Bacillus cereus*, and *Staphylococcus aureus*

18 samples tested for Norovirus by RT-PCR; 9 were positive
Challenges of Cafeteria Outbreaks

- Verifying Exposures
- Identifying potential healthy controls
- Finding people to interview them
- Hundreds of food items
- Rule in/out other exposures
Rapid Action

- Outbreak occurred toward end of week, right before Spring Break
- Sanitarians from local health department investigated, realized cafeteria was about to close for week and perform massive cleaning/maintenance
- Locked down all present food items, instructed staff not to throw anything out
Epidemiologic Investigation

- Unmatched Case-control study by Texas Dept. of Health
  - 36 ill subjects
  - 136 well controls

- Matched Case-control study by CDC
  - 29 ill subjects
  - 29 well controls
## Findings – Matched Study

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Odds Ratio</th>
<th>Confidence Intervals</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deli sandwich 3/9 lunch</td>
<td>11.0</td>
<td>1.6-473</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Deli sandwich 3/9 supper</td>
<td>6.0</td>
<td>0.7-276</td>
<td>0.06</td>
</tr>
<tr>
<td>Deli sandwich 3/10 lunch</td>
<td>8.0</td>
<td>1.1-355</td>
<td>0.02</td>
</tr>
<tr>
<td>Deli sandwich 3/10 supper</td>
<td>1.0</td>
<td>0.01-79</td>
<td>.75</td>
</tr>
</tbody>
</table>
# Findings – Unmatched Study

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Odds Ratio</th>
<th>Confidence Intervals</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deli sandwich 3/9 lunch</td>
<td>11.1</td>
<td>3.9-32</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Deli sandwich 3/9 supper</td>
<td>7.1</td>
<td>1.6-33</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Deli sandwich 3/10 lunch</td>
<td>5.7</td>
<td>2-16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Deli sandwich 3/10 supper</td>
<td>3.3</td>
<td>0.6-20</td>
<td>.11</td>
</tr>
<tr>
<td>Any deli sandwich on 3/9 or 3/10</td>
<td>16.8</td>
<td>6.2-47</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Interpretation

- Both studies implicated deli sandwiches on 3/9 and 3/10
- The more controls in a study, the better statistical power you have
- No other restaurants or food items showed any association
Sanitarians and epidemiologists interviewed foodhandlers.

All denied illness.

All except one submitted stool samples for testing.

One refused; cafeteria manager fired her.

She was responsible for slicing deli meats and making deli sandwiches.
Discussion

- CDC and TDH epidemiologists were disappointed with cafeteria manager decision to fire the one employee.
- Much more difficult to get cooperation.
- Eventually did interview her.
- She denied illness, but had infant with diarrhea.
- Stool sample from infant was PCR positive for Norovirus.
Researchers at Baylor College of Medicine agreed to try to find virus RNA on deli meat.

Never been done before.
Success!

- Lab successful in designing protocol for recovering virus RNA from deli meat
- Pulsed-Field Gel analysis of PCR results showed identical pattern between infant, ill students, and deli meats
Take Home Points

- Viral gastroenteritis is easy to spread
- Foodhandlers must be extremely careful, even when they are not sick, with hygiene
- It is possible to recover Norovirus from food
- Quick reaction by local health department sanitarians preserved food samples
- Collaboration with research lab advanced science of food safety research